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Docket No.: 17243/002001
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of:
Melwyn Abreo et al.

Patent No.: 7,763,618

Issued: July 27, 2010

22511
PATENT TRADEMARK OFFICE

For: PYRIDYL DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.323

ATTENTION: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Upon reviewing the above-identified patent, Patentee noted a typographical error which should be corrected.

In the Claims:

In Claim 29, Column 51, Line 47, "-$S(O)_2N(R^{12})2$" should read: "-$S(O)_2N(R^{12})_2$".

The error was not in the application as filed by applicant; accordingly no fee is required.

PAGE 2/10 * RCVD AT 10/4/2010 4:55:05 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-4/19 * DNIS:2738300 * CSID:7132288700 * DURATION (mm-ss):03-42

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Patent No.: 7,763,618 Docket No.: 17243/002001

Transmitted herewith is a proposed Certificate of Correction effecting such amendment. Also enclosed, as evidence of the error, is a copy of the claims as issued. Patentee respectfully solicits the granting of the requested Certificate of Correction.

Applicant believes no fee is due with this request. However, if a fee is due, please charge our Deposit Account No. 50-0591, under Order No. 17243/002001.

Dated: October 4, 2010

Respectfully submitted,

By _____

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PAGE 3/10 * RCVD AT 10/4/2010 4:55:05 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-4/19 * DNIS:2738300 * CSID:7132288700 * DURATION (mm-ss):03-42

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO.	:	7,763,618
APPLICATION NO.	:	10/566,857
ISSUE DATE	:	July 27, 2010
INVENTOR(S)	:	Melwyn Abreo et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

In Claim 29, Column 51, Line 47, "-$S(O)_2N(R^{12})2$" should read:

"-$S(O)_2N(R^{12})_2$".

MAILING ADDRESS OF SENDER (Please do not use customer number below):
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PAGE 4/10 * RCVD AT 10/4/2010 4:55:05 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-4/19 * DNIS:2738300 * CSID:7132288700 * DURATION (mm-ss):03-42

nate mitochondria and cellular debris. The supernatant is filtered through a 3-layer cheesecloth and centrifuged at 105,000×g for 60 min. The microsomal pellet is gently resuspended in the same homogenization solution with a small glass/teflon homogenizer and stored at −70° C. The absence of mitochondrial contamination is enzymatically assessed. The protein concentration is measured using bovine serum albumin as the standard.

Incubation of Mouse Liver Microsomes with Test Compounds:

Reactions are started by adding 2 mg of microsomal protein to pre-incubated tubes containing 0.20 μCi of the substrate fatty acid (1-^{14}C palmitic acid) at a final concentration of 33.3 μM in 1.5 ml of homogenization solution, containing 42 mM NaF_1 0.33 mM niacinamide, 1.6 mM ATP, 1.0 mM NADH, 0.1 mM coenzyme A and a 10 μM concentration of test compound. The tubes are vortexed vigorously and after 15 min incubation in a shaking water bath (37° C.), the reactions are stopped and fatty acids are analyzed.

Fatty acids are analyzed as follows: The reaction mixture is saponified with 10% KOH to obtain free fatty acids which are further methylated using BF_3 in methanol. The fatty acid methyl esters are analyzed by high performance liquid chromatography (HPLC) using a Hewlett Packard 1090, Series II chromatograph equipped with a diode array detector set at 205 nm, a radioisotope detector (Model 171, Beckman, Calif.) with a solid scintillation cartridge (97% efficiency for ^{14}C-detection) and a reverse-phase ODS (C-18) Beckman column (250 mmx4.6 mm i.d.; 5 μm particle size) attached to a pre-column with a μBondapak C-18 (Beckman) insert. Fatty acid methyl esters are separated isocratically with acetonitrile/water (95:5 v:v) at a flow rate of 1 mL/min and are identified by comparison with authentic standards. Alternatively, fatty acid methyl esters may be analyzed by capillary column gas-chromatography (GC) or Thin Layer Chromatography (TLC).

Those skilled in the art are aware of a variety of modifications to this assay that can be useful for measuring inhibition of stearoyl-CoA desaturase activity in microsomes by test compounds.

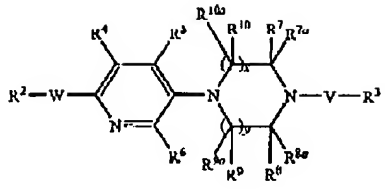
Representative compounds of the invention showed activity as inhibitors of SCD when tested in this assay. The activity was defined in terms of % SCD enzyme activity remaining at the desired concentration of the test compound.

All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet are incorporated herein by reference, in their entirety.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

The invention claimed is:

1. A method of inhibiting human stearoyl-CoA desaturase in vitro (hSCD) activity comprising contacting a source of hSCD with a compound of formula (I):



(I)

wherein:

x and y are each independently 1;

W is —C(O)N(R^1)— or —N(R^1)C(O)—;

V is —C(O)—;

each R^1 is independently selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{19}aralkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl, C_7-C_{19}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl, and C_3-C_{12}heteroarylalkyl;

R^3 is phenyl or naphthyl;

R^4, R^5 and R^6 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or —N(R^{13})$_2$;

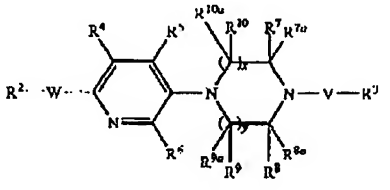
R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10} and R^{10a} are each independently selected from hydrogen or C_1-C_3alkyl;

and

each R^{13} is independently selected from hydrogen or C_1-C_6alkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof.

2. A method of alleviating a disease or condition mediated by stearoyl-CoA desaturase (SCD) in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



(I)

wherein:

x and y are each independently 1;

W is —C(O)N(R^1)— or —N(R^1)C(O) ;

V is C(O)—;

each R^1 is independently selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{19}aralkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl,

C_7-C_{12}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl, and C_3-C_{12}heteroarylalkyl;

R^3 is phenyl or naphthyl;

R^4, R^5 and R^6 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $—N(R^{13})_2$;

R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10} and R^{10a} are each independently selected from hydrogen or C_1-C_3alkyl; and

each R^{13} is independently selected from hydrogen or C_1-C_6alkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof,

and wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia, acne, and any combination of these.

3. The method of claim 2 wherein the mammal is a human.

4. The method of claim 3, wherein the disease or condition is Type II diabetes.

5. The method of claim 3, wherein the disease or condition is obesity.

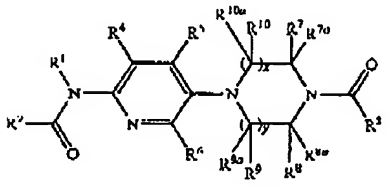
6. The method of claim 3, wherein the disease or condition is insulin resistance.

7. The method of claim 3, wherein the disease or condition is fatty liver.

8. The method of claim 3, wherein the disease or condition is non-alcoholic steatohepatitis.

9. A compound of formula (IIa):

(IIa)



wherein:

x and y are each independently 1;

R^1 is selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{19}aralkyl;

R^2 is selected from the group consisting of C_7-C_{12}alkyl, C_7-C_{12}alkenyl, C_7-C_{12}hydroxyalkyl, C_1-C_{12}alkoxy, C_2-C_{12}alkoxyalkyl, C_3-C_{12}hydroxyalkenyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_{13}-C_{19}aralkyl, C_1-C_{12}heteroaryl, C_3-C_{12}heterocyclylalkyl and C_3-C_{12}heteroarylalkyl, provided that R^2 is not pyrazinyl, pyridinonyl, pyrrolidinonyl or imidazolyl;

R^3 is phenyl or naphthyl;

R^4, R^5 and R^6 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $—N(R^{13})_2$;

R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each independently selected from hydrogen or C_1-C_3alkyl;

and

each R^{13} is independently selected from hydrogen or C_1-C_6alkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof

10. The compound of claim 9 wherein:

x and y are each 1;

R^1 is hydrogen or C_1-C_6alkyl;

R^2 is selected from the group consisting of C_7-C_{12}alkyl, C_7-C_{12}alkenyl, C_7-C_{12}hydroxyalkyl, C_7-C_{12}alkoxyalkyl, C_3-C_{12}hydroxyalkenyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_{13}-C_{19}aralkyl, C_3-C_{12}heterocyclylalkyl, and C_3-C_{12}heteroarylalkyl;

R^3 is phenyl or naphthyl;

R^4, R^5 and R^6 are each hydrogen; and

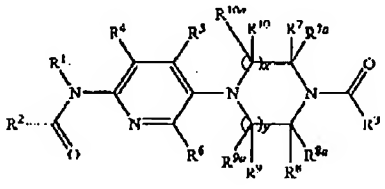
R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each hydrogen.

11. A method of alleviating a disease or condition mediated by stearoyl-CoA desaturase (SCD) in a mammal, wherein the method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 9, and wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia, acne, and any combination of these.

12. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 9.

13. A compound of formula (IIb):

(IIb)



wherein:

x and y are each independently 1;

R^1 is selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{19}aralkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_1-C_6alkoxy, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_7-C_{19}aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

or R^2 is phenyl optionally substituted with one or more substituents selected from halo and C_1-C_6trihaloalkyl;

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $-N(R^{12})_2$, $—C(O)R^{12}$, $—C(O)OR^{12}$, $S(O)_2N(R^{12})_2$, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl, provided that R^3 is not phenyl substituted with optionally substituted thienyl;

R^4, R^5 and R^6 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-N(R^{12})_2$;

R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each independently selected from hydrogen or C_1-C_3alkyl;

each R^{12} is independently selected from hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl; and

each R^{13} is independently selected from hydrogen or C_1-C_6alkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof.

14. The compound of claim 13 wherein:

x and y are each 1;

R^1 is hydrogen or C_1-C_6alkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_1-C_6alkoxy, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_7-C_{19}aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

or R^2 is phenyl optionally substituted with one or more substituents selected from halo or C_1-C_6trihaloalkyl;

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $—N(R^{12})_2$, $—OC(O)R^{12}$, $—C(O)OR^{12}$ and $—S(O)_2N(R^{12})_2$;

R^4, R^5 and R^6 are each hydrogen;

R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each hydrogen; and

each R^{12} is independently selected from hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl.

15. The compound of claim 14 wherein:

R^2 is C_7-C_{19}aralkyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_3alkyl and C_1-C_6trihaloalkyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

16. The compound of claim 15 selected from the group consisting of the following:

3-(4-Fluoro-phenyl)-N-{5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-propionamide;

4-Phenyl-N-{5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-butyramide;

4-(4-Fluoro-phenyl)-N-{5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-butyramide; and

3-Phenyl-N-{5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-propionamide.

17. The compound of claim 14 wherein:

R^2 is C_1-C_{12}alkyl or C_2-C_{12}alkenyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

18. The compound of claim 17 selected from the group consisting of the following:

Hexanoic acid {5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-amide;

Heptanoic acid {5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-amide; and 5-Methylpentanoic acid {5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-amide.

19. The compound of claim 14 wherein:

R^2 is C_1-C_{12}heteroarylalkyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_3alkyl and C_1-C_6trihaloalkyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

20. The compound of claim 19, namely, 3-Pyridin-3-yl-N-{5-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridin-2-yl}-propionamide.

21. The compound of claim 14 wherein:

R^2 is phenyl optionally substituted with one or more substituents selected from halo and C_1-C_6trihaloalkyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

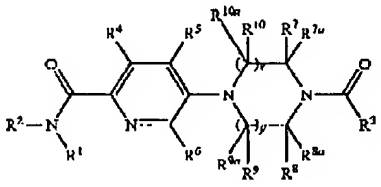
22. The compound of claim 21, namely, 4-Fluoro-N-{5-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridin-2-yl}benzamide.

23. A method of alleviating a disease or condition mediated by stearoyl-CoA desaturase (SCD) in a mammal, wherein the method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 13, wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia, acne, and any combination of these.

24. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 13.

25. A compound of formula (VIa):

(VIa)



wherein:

x and y are each independently 1;

R^1 is selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{19}aralkyl;

R^2 is selected from the group consisting of C_7-C_{19}alkyl, C_3-C_{12}alkenyl, C_7-C_{12}hydroxyalkyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}hydroxyalkenyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_{13}-C_{19}aralkyl, C_3-C_{12}heterocyclylalkyl, and C_3-C_{12}heteroarylalkyl;

R^3 is phenyl or naphthyl;

R^4, R^5 and R^6 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $—N(R^{13})_2$;

R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each independently selected from hydrogen or C_1-C_3alkyl;

and

each R^{13} is independently selected from hydrogen or C_1-C_6alkyl;

including a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof.

26. The compound of claim 25 wherein:

x and y are each 1;

R^1 is hydrogen or C_1-C_6alkyl;

R^2 is selected from the group consisting of C_7-C_{12}alkyl, C_3-C_{12}alkenyl, C_7-C_{12}hydroxyalkyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}hydroxyalkenyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_{13}-C_{19}aralkyl, C_3-C_{12}heterocyclylalkyl, and C_3-C_{12}heteroarylalkyl;

R^3 is phenyl or naphthyl;

R^4, R^5 and R^6 are each hydrogen; and

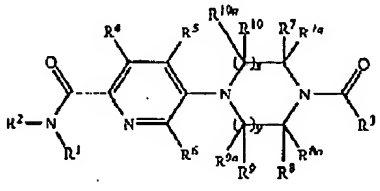
R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each hydrogen.

27. A method of alleviating a disease or condition mediated by stearoyl-CoA desaturase (SCD) in a mammal, wherein the method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 25, and wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia, acne, and any combination of these.

28. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 25.

29. A compound of formula (VIb):

(VIb)



wherein:

x and y are each independently 1;

each R^1 is independently selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{19}aralkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_3-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl, C_7-C_{19}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

R^3 is naphthyl or phenyl, each optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $-N(R^{12})_2$, $OC(O)R^{12}$, $C(O)OR^{12}$, $-S(O)_2N(R^{12})_2$, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl, provided that R^3 is not phenyl substituted with optionally substituted thienyl, and provided that when R^3 is naphthyl, R^2 can not be C_1-C_6alkyl, C_2-C_6hydroxyalkyl or phenyl substituted by amino;

R^4, R^5 and R^6 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-N(R^{12})_2$;

R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each independently selected from hydrogen or C_1-C_3alkyl;

each R^{12} is independently selected from hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl; and

each R^{13} is independently selected from hydrogen or C_1-C_6alkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof.

30. The compound of claim 29 wherein:

x and y are each 1;

R^1 is hydrogen or C_1-C_6alkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_3-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl, C_7-C_{19}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

R^3 is naphthyl or phenyl, each optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{12}$, $-C(O)OR^{12}$ or $-S(O)_2N(R^{12})_2$;

R^4, R^5 and R^6 are each hydrogen;

R^7, R^{7a}, R^8, R^{8a}, R^9, R^{9a}, R^{10}, and R^{10a} are each hydrogen; and

each R^{12} is independently selected from hydrogen, C_1-C_8alkyl, C_3-C_8cycloalkyl, aryl or aralkyl.

31. The compound of claim 30 wherein:

R^2 is C_7-C_{12}aralkyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_3alkyl and C_1-C_6trihaloalkyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

32. The compound of claim 31 selected from the group consisting of the following:

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid (3-phenyl-propyl)-amide;

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid phenethyl-amide;

5-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridine-2-carboxylic acid [2-(4-fluoro-phenyl)ethyl]amide;

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid [3-(4-fluoro-phenyl)-propyl]-amide;

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid 4-trifluoromethyl-benzylamide;

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid [3-(4-trifluoromethyl-phenyl)-propyl]-amide; and

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid [2-(4-trifluoromethyl-phenyl)-ethyl]-amide.

33. The compound of claim 30 wherein:

R^2 is C_1-C_{12}alkyl or C_2-C_{12}alkenyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

34. The compound of claim 33 selected from the group consisting of the following:

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid (3-methyl-butyl)-amide;

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid hexylamide;

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid pentylamide;

5-[4-(4-Fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid (3-methyl-butyl)-amide; and

5-[4-(5-Fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid (3-methyl-butyl)-amide.

35. The compound of claim 30 wherein:

R^2 is C_3-C_{12}cycloalkyl or C_4-C_{12}cycloalkylalkyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

36. The compound of claim 35 selected from the group consisting of the following:

5-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridine-2-carboxylic acid (3-cyclohexyl-propyl)amide;

5-[4-(6-Trifluoromethyl-cyclohexa-1,3-dienecarbonyl)-piperazin-1-yl]-pyridine-2-carboxylic acid (2-cyclohexyl-ethyl)-amide; and

5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carboxylic acid cyclohexylmethyl-amide.

37. The compound of claim 30 wherein:

R^2 is C_3-C_{12}heterocyclylalkyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $—N(R^{12})_2$, $—OC(O)R^{12}$, $—C(O)OR^{12}$ and $—S(O)_2N(R^{12})_2$;

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy; and

each R^{12} is independently selected from hydrogen, C_1-C_6alkyl, C_3-C_8cycloalkyl, aryl or aralkyl.

38. The compound of claim 37 wherein R^2 is 2-piperazinylethyl optionally substituted by $—C(O)OR^{12}$.

39. The compound of claim 38, namely, 4-[2-({5-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridine-2-carbonyl}-amino)-ethyl]-piperazine-1-carboxylic acid tert-butyl ester.

40. The compound of claim 30 wherein:

R^2 is C_7-C_{12}aralkyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_3alkyl and C_1-C_6trihaloalkyl; and

R^3 is naphthyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.

41. The compound of claim 40 selected from the group consisting of the following:

5-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-pyridine-2-carboxylic acid (3-phenyl-propyl)-amide; and

5-[4-(Naphthalene-1-carbonyl)piperazin-1-yl]pyridine-2-carboxylic acid phenethylamide.

42. A method of alleviating a disease or condition mediated by stearoyl-CoA desaturase (SCD) in a mammal, wherein the method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 29, wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia, acne, and any combination of these.

43. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 29.

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PTO/SB/97 (09-04)
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Application No. (if known): 10/566,857 Attorney Docket No.: 17243/002001

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